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14. ABSTRACT
Our goal is to develop a practical, diet-based intervention for prostate cancer. We have implemented a randomized clinical trial of a novel dietary intervention for prostate cancer that promotes vegetable intake among prostate cancer patients who are being treated with active surveillance. As part of this trial, we are testing whether a gene fusion biomarker will predict disease progression in this patient population. During the fourth year of the funding period, I accomplished eight major tasks. First, I oversaw the accrual of 150 patients at 40 sites nationally. Second, at the San Diego VA Hospital, I completed the required IRB documentation, opened the study to accrual, and recruited 10 patients. Third, I continued to oversee study enrollment at the Moores UC San Diego Comprehensive Cancer Center. Fourth, I responded to continued administrative review of the DoD human subjects protection documents. Fifth, I continued my regular participation in the Alliance for Clinical Trials in Oncology, formerly known as the Cancer and Leukemia Group B cooperative study group, by attending meetings and participating in conference calls. Sixth, I continued to guide the study protocol through regular contact with Alliance personnel, collaborators at participating sites, and revisions to the study protocol. Seventh, I presented a formal update of the study to Alliance clinical research associates. Finally, I presented a formal update of the study to the Southwest Oncology Group leadership.

15. SUBJECT TERMS
prostate cancer, diet, watchful waiting, active surveillance

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I. Introduction

Prostate cancer remains the most commonly diagnosed non-cutaneous cancer and the second leading cause of cancer death among U.S. men. In addition, accumulating data suggest that widespread population screening has prompted the indiscriminate, inappropriately aggressive treatment of early stage, low-grade prostate cancers with surgery or radiation, resulting in large numbers of prostate cancer survivors suffering from chronic, burdensome side effects that significantly decrease quality of life. These observations pose great challenges to the public health and call for the development of innovative approaches to prostate cancer prevention, control, and treatment.

One potential novel approach is dietary modification. Epidemiological and pre-clinical studies suggest that beneficial and specific alterations in nutritional intake may protect against prostate cancer initiation and progression. However, despite widespread public interest in this topic, there are very few clinical studies investigating the potential benefits of diet-based interventions for prostate cancer.

We have successfully developed and pilot tested a telephone-based dietary intervention for prostate cancer patients based on well-established principles of social cognitive theory.[1,2] This relatively straightforward, low-cost intervention—which utilizes behavior modification to increase vegetable intake and decrease fat intake—is the first to utilize diet as a form of primary clinical therapy for prostate cancer. Due to its practicality, simplicity, and proven benefits to cardiovascular and overall health, this intervention would be widely applicable. Use in an active surveillance ("watchful waiting") population may potentially spare thousands of patients each year from the considerable side effects of surgery and radiation.

We hypothesize that a vegetable-intense diet will decrease disease progression and improve quality of life in men with prostate cancer. Our goal is to develop a practical, diet-based intervention for prostate cancer. We have implemented a national, randomized clinical trial of a novel dietary intervention—the Men's Eating and Living (MEAL) study—that utilizes a central, telephone-based counseling program to promote vegetable intake among prostate cancer patients who are being treated with active surveillance. As part of this trial, we are testing whether a gene fusion biomarker will predict disease progression in a sub-group of patients.

Notably, the MEAL study is the first national, Phase III trial designed to test a diet-based intervention for prostate cancer and the first non-industry sponsored trial designed to test an intervention of any kind in prostate cancer patients on active surveillance. As such, it holds the potential to substantially inform treatment paradigms for prostate cancer, particularly in patients with early stage, less aggressive forms of this disease.

II. Body

Progress to Date

During the fourth year of the funding period, I made substantial progress in 8 specific areas, fulfilling all of the major goals posted in the last annual report.

1) Accrual of patients to study

Through phone calls, e-mail correspondence, presentations, and face-to-face meetings, I have personally overseen the expansion of the study and recruited additional sites to participate. As of September 28, 2012 a total of 185 patients had been enrolled and 143 randomized to study, with an additional 9 still in the run-in period (**Appendix**). A total of 40 different sites across the nation are now open to accrual, with additional sites opening each month. These data represent a large increase in accrual since the last annual report, at which time only 28 patients had been randomized. With the increased number of study sites, the pace of accrual has recently quickened, with approximately 15 patients currently randomized to study each of the last 6 months. The planned number of study participants is 464; thus, over the last year, I have made substantial progress toward this goal.

2) Opening of the study at the San Diego VA Hospital

At the San Diego VA Hospital, at which I am an attending physician who regularly participates in the clinical care of prostate cancer patients, I completed the required local IRB documentation, opened the study to accrual, and recruited 10 patients to study. I have personally designed and implemented the process by which potential study participants are prospectively identified, screened, and recruited to study.

3) Study enrollment at the Moores UC San Diego Comprehensive Cancer Center

At the Moores UC San Diego Comprehensive Cancer Center, at which I am an attending physician who regularly participates in the clinical care of prostate cancer patients, I continued to oversee identification, screening, and recruitment of patients. During the reporting period, we recruited an additional 17 patients to study, making UC San Diego one of the top accruing sites nationally.

4) Response to routine human subjects protection administrative review.

I successfully responded to the annual administrative review of the DoD human subjects protection documents and to the annual local IRB reviews at the San Diego VA Hospital and the UC San Diego Comprehensive Cancer Center.

5) Participation in the Alliance for Clinical Trials in Oncology

I continued my regular participation in the Alliance for Clinical Trials in Oncology (formerly known as the Cancer and Leukemia Group B cooperative study group) by

attending meetings, conferring with Alliance leadership, participating in regular conference calls, and engaging in email correspondence. At Alliance meetings on March 17, 2012 and June 29, 2012 in Chicago, I presented formal updates of the study to the Alliance membership.

6) Oversight of the national study protocol

I continued to guide the study protocol through regular contact with Alliance personnel and collaborators at participating sites. I oversaw several formal revisions to the study protocol, including but not limited to clarification of the inclusion/exclusion criteria, addition of an exclusion criterion for patients taking a class of medications known as 5-alpha reductase inhibitors, and revision of the follow-up prostate biopsy protocol.

7) Formal presentation at the Alliance for Clinical Trials meeting

I made a formal presentation discussing the study to over 100 Alliance for Clinical Trials in Oncology clinical research associates and research nurses in Chicago on November 18, 2011. The title of the presentation was, "The Men's Eating and Living (MEAL) Study (CALGB 70807): A Randomized Trial of Dietary Intervention in Men on Active Surveillance for Prostate Cancer."

8) Formal presentation to the Southwest Oncology Group meeting

I made a formal, invited presentation of the study to the Southwest Oncology Group genitourinary cancers team leadership in San Francisco on April 14, 2012. The title of the presentation was, "The Men's Eating and Living (MEAL) Study (CALGB 70807): An Update." As part of this presentation, I answered questions regarding the aims and conduct of the study, and I participated in a discussion of the future of clinical trials in prostate cancer patients on active surveillance programs.

Problem areas

There are no current problems impeding performance. The trial is accruing patients at a steady pace, and accrual is accelerating at this time.

The original grant timeline estimated that the trial would open to accrual in March 2009. With the additional time required to secure funding and guide the CALGB protocol through the review processes, the trial remains at least 24 months behind the original projected schedule. The timeline will require revision to account for this delay; however, the new timeline will depend in part as to how quickly the accrual goal of 464 patients is met.

As accrual continues to accelerate with the addition of new sites each month, it is difficult to project at this time how quickly the study will accrue. Nevertheless, it is highly likely, if not certain, that the trial will not finish prior to the 5-year funding period.

It is worth noting, however, that the initial delays in opening the trial resulted directly from the unexpected, yet highly fortunate, opportunity that arose for expanding the study from its original two-site pilot design to a national trial involving hundreds of additional patients from at least 40 different sites.

Over the next year, I will work closely with Dr. Melissa Cunningham, my scientific officer, to anticipate any additional changes, identify the final timeline, and design a plan for submitting Reportable Outcomes beyond the 5-year funding period.

Work to be performed during next reporting period

I have five goals for the next reporting period:

1) *Continue to accrue patients to study at the Moores UCSD Cancer Center.*

2) *Continue to accrue patients to study at the San Diego VA.*

3) *Continue oversight of the national study protocol.*

4) *Continue to open new sites for the enrollment of patients.*

5) *Complete the first planned interim analysis of baseline prostate biopsy data, report of which will constitute a Reportable Outcome.*

6) *Submit a manuscript describing the study to the peer-reviewed journal* Contemporary Clinical Trials*, successful publication of which would constitute a Reportable Outcome.*

7) *Continue planning of a new study timeline depending upon how quickly patients accrue to study, particularly over the time period September 20, 2012 to March 31, 2013.*

III. Key Research Accomplishments

- Successful accrual and randomization of patients.
    - A total of 185 patients recruited and 143 randomized to study as of September 30, 2012.

- Recruitment of an additional 17 patients to study at the UC San Diego Moores Cancer Center.

- Opening of the study and recruitment of 10 patients to study at the San Diego VA Hospital.

- Successful response to ongoing administrative review of DoD, UC San Diego, and San Diego VA Hospital human subjects protection protocols.

- Continued participation in Alliance for Clinical Trials in Oncology (known formerly as Cancer and Leukemia Group B) activities, including conference calls, meetings in Chicago to update Alliance leadership on the status of the trial, and formal presentations to Alliance personnel.

- Successful continued oversight of the study protocol, including but not limited to:
    - Regular correspondence with Alliance personnel and collaborators at participating sites across the U.S.
    - Design and implementation of several protocol amendments, including but not limited to clarification of the inclusion/exclusion criteria, addition of an exclusion criterion for patients taking a class of medications known as 5-alpha reductase inhibitors, and revision of the follow-up prostate biopsy protocol.
    - Resolution of numerous questions and practical issues posed by study coordinators and collaborators at participating sites

- Recruitment of additional sites, with 40 sites currently participating across the U.S.

IV. Reportable Outcomes

There were no reportable outcomes during the study period. Because the trial is still accruing patients, there are no data to report at this time. However, I anticipate results from the first planned interim analysis within the next 2 months.

V. Conclusion

In summary, I achieved substantial progress during the fourth year of the funding period, meeting all of the major goals outlined in the previous annual report.

I oversaw the accrual of 150 patients at 40 sites nationally; opened the study to accrual at the San Diego VA Hospital and enrolled 10 patients; continued to oversee study enrollment at the Moores UC San Diego Comprehensive Cancer Center and enrolled an additional 17 patients; successfully responded to continued administrative review of the DoD, Moores UC San Diego, and San Diego VA Hospital human subjects protection documents; continued my regular participation in the Alliance for Clinical Trials in Oncology, formerly known as the Cancer and Leukemia Group B cooperative study group; continued to lead the national study protocol by coordinating regular contact with Alliance personnel, collaborators at participating sites, and revisions to the study protocol; presented a formal update of the study to Alliance clinical research associates entitled, “The Men’s Eating and Living (MEAL) Study (CALGB 70807): A Randomized Trial of Dietary Intervention in Men on Active Surveillance for Prostate Cancer;” and, finally, I presented a formal update of the study to the Southwest Oncology Group leadership entitled, “The Men’s Eating and Living (MEAL) Study (CALGB 70807): An Update.”

Due to the unexpected expansion of the study to a national, randomized clinical trial involving hundreds of additional patients, the trial remains behind the original estimated timeline. However, the trial is currently accruing well, without barriers to performance, and substantial Reported Outcomes are anticipated.

IV. References

1. Parsons JK, Newman V, Mohler JL, Pierce JP, Flatt S, and Marshall J. Dietary modification in prostate cancer patients on active surveillance: a randomized, multi-center feasibility study. BJU Int, 101: 1227-1231, 2008.

2. Parsons JK, Newman V, Mohler J, Pierce JP, Paskett E, and Marshall J. The Men's Eating and Living (MEAL) Study: A Cancer and Leukemia Group B pilot trial of dietary intervention for the treatment of prostate cancer. Urology, 72: 633-7, 2008.

V. Appendix

Summary of accrual data for the Men's Eating and Living (MEAL) study (CALGB 70807) as of September 29, 2012.

MEAL Recruitment Report

9/28/2012

Sub Site ID	Sub Site Accr	Sub Site Name	Total to Date							From: **9/1/12** to **9/28/12**			
			Recruit	Random	Run In With drew	Run In Not Eligible	Still In Run In	Study With drew	Study Completed	Recruit	Randomized	Run In With drew	Run In Not Eligible
85	AKRON	Akron Cancer Research	1	1	0	0	0	0	0	0	0	0	0
121	BAYO	Bay Area Hospital	1	1	0	0	0	0	0	0	0	0	0
86	BEAU	Beaumont CCOP	4	4	0	0	0	0	0	0	0	0	0
99	BIRD	Mary Bird Perkins Cancer C	4	3	0	1	0	0	0	0	0	0	0
87	CEDAR	Cedars-Sinai Cancer Cente	1	0	0	1	0	0	0	0	0	0	0
88	CHRIS	Christiana	2	2	0	0	0	0	0	0	0	0	0
89	CLEV	Cleveland Clinic Florida	5	3	0	1	1	0	0	1	0	0	0
90	CORN	Cornell	2	2	0	0	0	0	0	0	0	0	0
91	DANA	Dana Farber	2	2	0	0	0	0	0	0	0	0	0
122	ELLE	Elliott Hospital	1	0	0	1	0	0	0	0	0	0	0
92	GEOR	Georgetown	5	5	0	0	0	0	0	1	1	0	0
93	GRCOP	Grand Rapids Clinical Onco	1	1	0	0	0	0	0	0	0	0	0
94	HIGH	High Point Regional	4	4	0	0	0	0	0	0	1	0	0
113	HUNT	U Utah-Huntsman	10	8	0	2	0	0	0	0	0	0	0
124	LAKE	Lakeland Regional Cancer	1	0	0	1	0	0	0	0	0	0	0
74	M2UC	UCSD MEAL2 Study Subsi	27	17	2	8	0	0	0	0	0	0	0
75	M2VA	VA Hospital MEAL2	10	8	0	1	1	0	0	1	0	0	0
127	MADI	Madigan Army Medical Cer	1	1	0	0	0	0	0	1	1	0	0
117	MASON	Virginia Mason	7	4	1	0	1	0	0	1	1	0	0
123	MAYO	Mayo Clinic	1	0	1	0	0	0	0	0	0	0	0
125	MICH	Michigan Cancer Research	1	1	0	0	0	0	0	0	0	0	0
95	MUIR	John Muir Health	2	2	0	0	0	0	0	0	0	0	0
129	NAVY	Navy Medical Center San D	2	0	0	0	2	0	0	2	0	0	0
100	NCRF	Nevada Cancer Institute Fo	10	8	0	2	0	0	0	0	0	0	0
101	NSJEW	North Shore Jewish Health	2	1	0	1	0	0	0	0	0	0	0
102	POUD	Poudre, CO	1	0	0	1	0	0	0	0	0	0	0
103	RPCI	Roswell Park	20	19	0	1	0	0	0	0	0	0	0
131	Sinai	Mt. Sinai School of MEdicin	1	0	0	0	1	0	0	1	0	0	0
105	SOREG	Southern Regional Medical	1	0	1	0	0	0	0	0	0	0	0
106	STEEP	Steeplechase	3	3	0	0	0	0	0	0	0	0	0
107	TRIN	Trinity Health-St. Joseph M	6	5	0	1	0	0	0	0	0	0	0
108	UCHIC	U Chicago	10	7	0	3	0	0	0	0	0	0	0
115	UCSF	UC San Francisco	3	3	0	0	0	0	0	0	0	0	0
109	UKAN	U Kansas	2	2	0	0	0	0	0	0	0	0	0
110	UKENT	U Kentucky	1	1	0	0	0	0	0	0	0	0	0
111	UPENN	U Pennsylvania	6	5	0	1	0	0	0	0	0	0	0
112	UTEX	U Texas	3	2	0	1	0	0	0	0	0	0	0
114	UVERM	U Vermont	5	5	0	0	0	0	0	0	0	0	0
116	VAKC	VA-Kansas City	1	0	0	0	1	0	0	1	0	0	0
118	WASH	Washington University	11	11	0	0	0	0	0	0	0	0	0
126	WINT	Winter Park Urology	4	2	0	0	2	0	0	2	2	0	0
		Total All Sites	**185**	**143**	**5**	**27**	**9**	**0**	**0**	**11**	**6**	**0**	**0**